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Use of lipids peroxidized for the preparation of a pharmaceutical composition; RTI ID=1.1> cutéique< /RTI> intended for the treatment by local application of the télangiectasies
The present invention relates to a new therapeutic indication of known products, and primarily has as an aim the use of lipids peroxidized for the preparation of a pharmaceutical composition intended for the treatment by local application of the télangiectasies.

Les télangiectasies, still called varicosities, appear primarily by marks or features red or blue, according to whether they are arterial or venous, on the skin.

These demonstrations are the consequence of a circulatory phenomenon whose etiology at present is very discussed but which is related to a phenomenon of circulatory hyperpression. At present, the only known treatment of these varicosities is a treatment says "bloody" treatment which consists in sclerosing them.

< RTI ID=1.2> 11< /RTI> was discovered now, and this constitutes the base of this invention, that certain peroxidized lipids have a very great effectiveness to treat, in local application, the télangiectasies.

Thus, the present invention has as an aim the use of peroxidized lipids showing a rate of peroxidation ranging between 50 and 200 milliéquivalents per kilo, preferably between 50 and 150 milliéquivalents per kilo, for the preparation of a pharmaceutical composition intended for the treatment, by local application, of the télangiectasies.

The peroxidized lipids used in accordance with the invention are known products prepared starting from lipids for example by oxygen saturation and exposure intensive and controlled to the ultraviolet rays.

These products were in particular described in the documents < RTI ID=1.3> BSM< /RTI> 2330 M, EP-A-293 535, < RTI ID=1.4> FR-A-2591112< /RTI> < RTI ID=1.5> ; EP-A-225 831< /RTI> EP-A-225 832; EP-A-225 833; < RTI ID=1.6> EP-A-226 506; < /RTI> FR-A-2 < RTI ID=1.7> 461744< /RTI> FR-A-2 < RTI ID=1.8> 539142< /RTI> and EP-A-117 962.

In these former documents, these compounds are presented like likely to be used in the treatment of certain affections, in particular in rheumatology or traumatology, or as a healing product.

More recently, it was discovered that the local application of these products is likely to increase in a remarkable way, not only surface blood flow, but also subcutaneous or major blood flow.

This new application of the peroxidized lipids is described in the patent EP 0.480.983 which describes a new fashion of treatment of the insufficiencies circutoires. However, this document does not comprise any indication concerning the particular problem of the treatment of the télangiectasies since it proposes a new treatment of the circulatory phenomena related to an insufficient blood flow and not of those related to a too strong pressure.

Likely peroxidized lipids < RTI ID=2.1> de être< /RTI> used in accordance with the invention can be of very varied nature chemical. They show a rate of peroxidation, measured by method AFNOR, ranging between 50 and 200 milliéquivalents per kilo, and preferably between 50 and 150 milliéquivalents per kilo.

According to a particular mode of realization, these lipids present a content of glycérides advantageously oxidized ranging between 5 and 40%.

In accordance with the invention, one uses preferentially as lipid peroxidized at least a peroxide obtained by peroxidation of lipids of vegetable origin, for example in the form of with less one natural vegetable oil. Preferably, these oils are selected among the sweet almond oil, the hazel nut oil, the groundnut oil, the corn oil, the oil of grape pip, the sesame oil and the oil of carthame.

According to a particular mode of realization of the invention, one uses peroxidized lipids made up mainly or mainly of triglycerides answering the general formula: < RTI ID=2.2> CH₂-O-R< /RTI>
CH-O-R

CH₂-O-R in which the radicals R are < RTI ID=2.3> majoritairement< /RTI> represented by the acids < RTI ID=2.4> octadécanoïques< /RTI> and < RTI ID=2.5> octadécanoïques< /RTI> peroxidized.

According to a particular characteristic of the invention, these products are used for the preparation of a pharmaceutical composition intended to be applied locally, and are presented in a general way in the shape of a cream, of a gel. One can also consider compositions being presented in the form of liquid, or in the form of soft capsule containing the peroxidized lipids.

A pharmaceutical composition thus prepared includes/understands, expressed in percentages by weight, 2 to 99% of peroxidized lipids, approximately < RTI ID=2.6> 1% < /RTI> of perfume, as well as pharmaceutically acceptable

Advantageously, this pharmaceutical composition is presented in the form of a cream containing:

- cetyl alcohol 2,0%
- acid stearic 5,0%
- peroxidized lipids 25,0%
- silicones < RTI ID=3.1> 0,5% < /RTI>
- propylenglycol 3,0%
- < RTI ID=3.2> triethanolamine< /RTI> 0,2 %
- perfume < RTI ID=3.3> 0,8% < /RTI>
- emulsifier nonionic 6,0%
- antimicrobial 0.3%

- demineralized water q.s.p. 100

The effect of the peroxidized lipidic compounds used in topical application in accordance with the present invention to treat the telangiectasias was highlighted not only by direct visual examination but still by a photographic examination intended to evaluate the bleaching of the varicosities after treatment by the aforementioned compounds.

Example 1

Preparation of a pharmaceutical composition containing peroxidized lipids, coming from an oil of carthame virgin available in the trade.

Oil of carthame virgin available in the trade showing the following principal characteristics:

- peroxide index 18,70 méq. /kg
 - glycéride oxidized 4,18%
 - viscosity with γ RTI ID=3.4> 50-C< /RTI> 23,2.10-6 m2/s (23,2 centistoke) is subjected to a treatment of peroxidation as described in the document
- FR-A-2 < RTI ID=3.5> 461744 < /RTI>

This process consists in storing the oil of carthame in a tank out of stainless steel. This tank is capped with a hood swivelling able to collect the vapors and being used as support with a lamp with ultraviolet radiation, for example PHILIPS type HP 4 of 125 W.

This tank is supplied uninterrupted by an air pump for example with a flow of < RTI ID=4.1> 30 l/min/< /RTI> to obtain an effect of splashing. The tank is also heated by the resistances fed while electrical current in order to maintain a temperature of 80 with < RTI ID=4.2> 100il.< /RTI>

Oil is thus maintained for one duration from 20 to 35 H according to Iorigine of the lipids, in particular 25 H for the oil of carthame considered in this example, in order to obtain a rate of peroxidation in conformity with the invention.

The oil thus obtained after peroxidation is stored in a storage tank which receives oil of carthame peroxidized being able to come from several tanks of peroxidation.

The oil of carthame peroxidized obtained by the process pointed out above shows the following principal characteristics:

- peroxide index 149,0 méq. /kg
- glycéride oxidized 11,30%
- viscosity with $\langle RT \rangle$ ID=4.3> 50iC< /RT> 25.9.10⁻⁶ m²/s (25.9 centistoke)

From this peroxidized oil, one can prepare capsules with soft wall encapsulating the oil of carthame peroxidized and releasing the oil of carthame peroxidized during a topics application, by massage.

With this intention, one can encapsulate the oil of carthame peroxidized by all proceeded traditional of encapsulation in a soft capsule whose tunic is carried out mainly with a gelatine-water mixture/glycerin, the respective composition of the contents of the soft capsule and tunic of the capsule being as follows for example for a batch of 635,415 kg making it possible to prepare 600.000 capsules in multiple and submultiple:

With - Contents of the soft capsules

- oil of carthame peroxidized 136,800 kg
 - perfume anise 3,00 kg
 - silica colloidal 10,200 kg
- 150,000 kg
- B - Tunic (wall of the soft capsules)
- gelatine 211,796 kg
 - glycerin 106,357 kg
 - purified water 164,147 kg
- < RTI ID=5.1 > - bioxyde< /RTI> of titanium 2,414 kg
- 485,415 kg

The machine used makes it possible for example to prepare soft capsules of 460 Mg having thus the following composition:

Contents mg/capsule

Oil peroxidized carthame 228,000 Mg

Perfume anise ref. 9/500918 5,000 Mg

Silica colloidal 17,000 Mg

For contents of 250,000 Mg

Tunic 210,000 Mg + 10%

Titanium 0,75% dioxide

Mix gelatine-water/glycerin (67/33) q.s. % $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$
for a capsule of < RTI ID=5.2> 460,000 Mg + 5% < /RTI>

Example 2

A multicentric clinical study was carried out on 60 patients presenting of the varicosities on the lower limbs.

The product tested in this example is a peroxidized corn oil showing a rate of peroxidation of 110 milliequivalents per kilo.

The test was carried out in the following way:

- Application: $\langle RTI \text{ ID} = 5.3 \rangle$: $\langle /RTI \rangle$ twice a day by light massages of the product applied by touches at a rate of 10 to 15 drops per localization.

- Course of the study

. The product is used in monothérapie.

. $\langle RTI \text{ ID} = 6.1 \rangle$ Ltévaluation $\langle /RTI \rangle$ was made after 6 weeks of treatment.

$\langle RTI \text{ ID} = 6.2 \rangle$. Les $\langle /RTI \rangle$ results on the bleaching of the varicosities are evaluated by the practitioner attending in agreement with the testimony of the patient.

One on average observes in the majority of the cases a discolouration of the varicosities, apparent at the end of 30 days.

This examination was supplemented by a photographic examination intended to compare the intensity of colouring of the varicosities before and after the treatment.

This photographic examination was carried out by taking all the photographs under the same conditions (160 ASA, 45 cm, through a fixed fluorescent lamp).

The results obtained after 30 days of treatment for each patient were related to a tick-marked line where item 0 represents the conditions of the patient before the treatment and item 10 the complete disappearance of the varicosities.

The average result ranges between 7 and 8.